

# Anti-GQ1b Antibody Syndrome Presented as Locked-In Syndrome: A Rare Case Report

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Review began 09/18/2023

Review ended 11/27/2023

Published 12/03/2023

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## Abstract

Anti-GQ1b antibodies are considered a hallmark of Miller-Fisher syndrome (MFS), a rare variant of Guillain-Barré syndrome (GBS). The typical clinical presentation of MFS includes ophthalmoplegia, ataxia, and areflexia. Here, we present an unusual case of a 65-year-old man with acute-onset quadriplegia and bulbar weakness resembling locked-in syndrome. Imaging studies did not show structural lesions as a cause for his clinical symptoms. Nerve conduction studies showed severe axonal sensory-motor polyneuropathy. Serum studies were all negative except for a positive anti-GQ1b antibody. He was treated with plasmapheresis as MFS, with a quick improvement in muscle strength. Our case report provided further information on the clinical variation of anti-GQ1b syndrome. Physicians should pay more attention to unusual presentations of anti-GQ1b syndrome because, when it is recognized early with prompt treatment, patients are expected to have a good recovery.

**Categories:** Neurology

**Keywords:** locked-in syndrome, guillain-barre syndrome (gbs), anti-gq1b, miller fisher syndrome, bulbar palsy

## Introduction

Miller-Fisher syndrome (MFS), a rare variant of Guillain-Barré syndrome (GBS), is characterized by the acute onset of ophthalmoplegia, ataxia, and areflexia. The anti-GQ1b antibody was first discovered in typical Miller-Fisher syndrome in 1992 [1] and has been considered a hallmark of the diagnosis. Several other clinical syndromes, such as Bickerstaff brainstem encephalitis (BBE), acute ophthalmoplegia, and even GBS, have been reported to be associated with anti-GQ1b antibodies. Thus, anti-GQ1b antibody syndrome was proposed in later literature [2]. Anti-GQ1b syndrome is divided into six types according to the clinical manifestations: typical MFS, incomplete MFS, GBS, BBE, acute ophthalmoplegia, and pharynx-neck-brachial muscle weakness [3]. It is not uncommon that patients may have an incomplete clinical presentation for each syndrome or can present with overlapping syndromes.

Bulbar involvement is not part of the triad that MFS clinically presents with and is easily overlooked. When a patient presents with acute-onset severe weakness that includes bulbar involvement, it can resemble locked-in syndrome. Locked-in syndrome (LIS) is a condition often resulting from brain stem damage that commonly presents with quadriplegia and bulbar palsy with preserved vertical eye movements, blinking, and hearing. Patients with the incomplete form of LIS may have some preserved motor function, such as horizontal eye movement or facial expression. The most common cause of LIS is vascular complications to the brain stemming from hemorrhagic or ischemic strokes. Following that, traumatic injuries to the brainstem are the second most common cause of LIS [4]. Peripheral conditions may have clinical features similar to LIS, such as acute GBS, myasthenia gravis, and critical illness neuropathy/myopathy.

Here, we present a case of acute-onset quadriplegia with bulbar palsy resembling LIS secondary to a positive anti-GQ1b antibody and a good response to plasma exchange therapy.

## Case Presentation

A 65-year-old man with a past medical history of HTN, alcohol abuse, liver cirrhosis, and pAfib was admitted to our hospital due to unresponsiveness secondary to *Escherichia coli* urosepsis and hepatic encephalopathy that required pressors and ventilatory support. His medical condition quickly improved within the first few days following intubation; however, he was still "unresponsive," and neurology was consulted. On his first neurologic examination, he was able to move his eyes to sound stimulation and track providers with his eyes but was without verbal output. He was able to respond to some commands, including raising his eyebrows and blinking. His horizontal eye movements were intact while tracking the examiner. He was not able to show facial expressions and could barely open his mouth. All four limbs were flaccid. Patellar and Achilles reflexes were absent, but deep tendon reflexes on the upper extremities were preserved. The sensory exam was limited due to minimal communication. A cerebellar exam was unable to be obtained due to severe quadriplegia. Neuropathy labs were unremarkable (Table 1). Brain and cervical spine magnetic resonance imaging (MRI) was unremarkable, with no structural lesions such as pontine stroke or central pontine myelinolysis as possible causes for his quadriplegia (Figures 1-3). Nerve conduction studies demonstrated

### How to cite this article

D'Angelo K M, Williams J, Wu L (December 03, 2023) Anti-GQ1b Antibody Syndrome Presented as Locked-In Syndrome: A Rare Case Report. Cureus 15(12): e49866. DOI 10.7759/cureus.49866

severe generalized sensory-motor polyneuropathy with axonal loss (Figures 4, 5). F-waves from lower limbs were not recordable due to absent sensory and motor M-responses (Figure 6). In the upper limbs, F-waves were absent in the median nerve and severely reduced persistence in the ulnar nerve. The antiganglioside antibody panel revealed a positive anti-GQ1b antibody with an anti-Gq1b titer of 60IV (ref: 0-50). All other antiganglioside antibodies, including anti-GM1, were negative. The patient was treated with five cycles of plasmapheresis. His muscle strength started to improve after the second plasma exchange, and all neurological symptoms continued to improve throughout the treatment. After completing the course, he was able to lift both legs against gravity. He was able to converse with simple verbal output. Upon discharge, he was able to sit up. His muscle strength continued to improve after discharge, and it was documented on a follow-up visit that he was able to stand up without assistance.

Lab	Result	Units
B1	253	nmol/L
Folate	10	ng/mL
B12	922	pg/mL
TSH	0.09	mIU/L
Free T3	2.94	pg/mL
Free T4	1.20	ng/dL
Glucose	121	mg/dL
HCV Ab	Negative	--
HCV Semi-Quantitative	0.02	--
HBsAb	Negative	--
HBsAb Semi-Quantitative	0.00	mIU/mL
HBsAg	Negative	--
HBsAg Semi-Quantitative	0.09	--
HIV	Negative	--

TABLE 1: Neuropathy work-up lab results

A neuropathy lab workup is shown above. Several attempts at a lumbar puncture were unsuccessful.

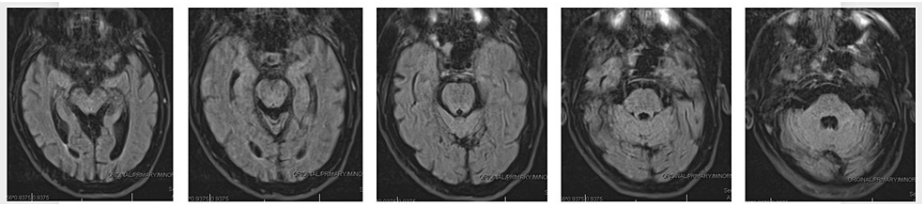
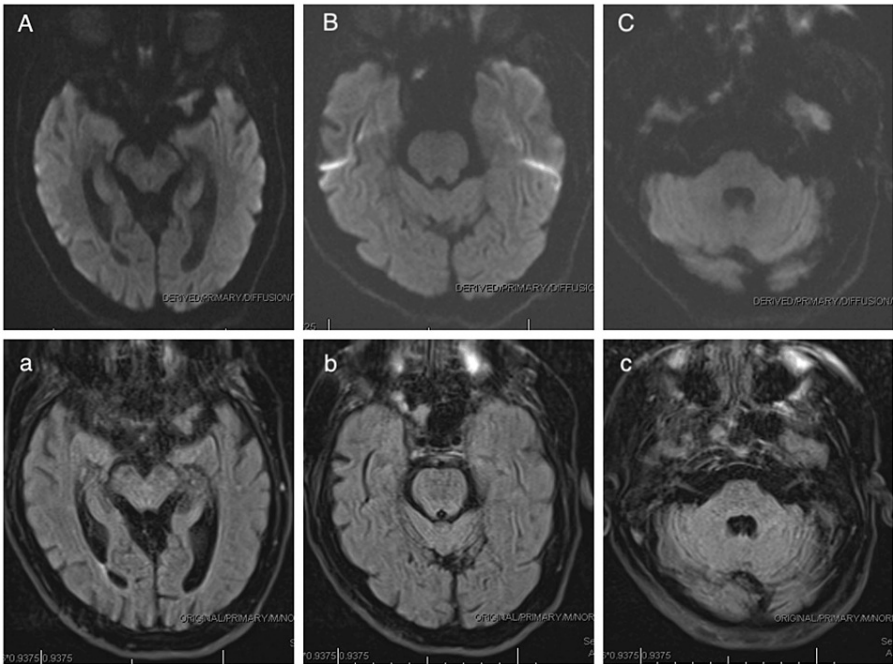


FIGURE 1: Brain MRI FLAIR

The patient's brain MRI did not show abnormalities.



**FIGURE 2: MRI DWI**

Upper A, B, C: DWI, lower a. b. c: FLAIR



**FIGURE 3: C-spine MRI T2**

No abnormalities were noted on the patient's C-spine when imaged on an MRI.

Sensory - Upper Summary Table

Stim Site	NR	Peak (ms)	Norm Peak (ms)	O-P Amp (µV)	Norm O-P Amp	Site1	Site2	Delta-P (ms)	Dist (cm)
Left Median Anti Sensory - Upper (2nd Digit)									
Wrist		3.1	<3.6	4.4	>15	Wrist	2nd Digit	3.1	14.0
Elbow		3.1		6.0		Elbow	Wrist	0.0	0.0
Left Radial Anti Sensory - Upper (Base 1st Digit)									
Wrist		2.0	<2.9	19.9	>20	Wrist	Base 1st Digit	2.0	0.0
Left Ulnar Anti Sensory - Upper (5th Digit)									
Wrist		3.9	<3.1	5.7	>10	Wrist	5th Digit	3.9	14.0

Sensory - Lower Summary Table

Stim Site	NR	Peak (ms)	Norm Peak (ms)	O-P Amp (µV)	Norm O-P Amp	Site1	Site2	Delta-P (ms)	Dist (cm)
Left Sup Peron Anti Sensory - Lower (Ant Lat Mall)									
14 cm	NR		<4.1		>5.0	14 cm	Ant Lat Mall		14.0
Left Sural Anti Sensory - Lower (Lat Mall)									
14cm	NR		<4.5		>6.0	14cm	Lat Mall		14.0

FIGURE 4: Upper and lower extremity sensory nerve summary table

There is reduced amplitude shown in the sensory nerves of both upper and lower extremities, suggesting polyneuropathy with axonal loss.

Motor - Upper Summary Table

Stim Site	NR	Onset (ms)	Norm Onset (ms)	O-P Amp (mV)	Norm O-P Amp	iAmp (mV)	Neg Dur (ms)	Neg Area (mVms)	Site1	Site2	Delta-0 (ms)	Dist (cm)	Vel (m/s)	Norm Vel (m/s)
Left Median Motor - Upper (Abd Poll Brev)														
Wrist		3.2	<4.0	4.6	>6.0	5.4	7.50	19.99	Elbow	Wrist	5.7	24.0	42	>48
Elbow		8.9		3.6		4.2	7.73	15.77						
Left Ulnar Motor - Upper (Abd Dig Minimi)														
Wrist		2.8	<3.6	3.6	>6	4.0	7.66	14.42	B Elbow	Wrist	3.3	22.0	67	>51
B Elbow		6.1		3.2		3.6	8.83	15.32	A Elbow	B Elbow	3.5	12.0	34	>51
A Elbow		9.6		3.1		3.4	8.75	15.36						

Motor - Lower Summary Table

Stim Site	NR	Onset (ms)	Norm Onset (ms)	O-P Amp (mV)	Norm O-P Amp	iAmp (mV)	Neg Dur (ms)	Neg Area (mVms)	Site1	Site2	Delta-0 (ms)	Dist (cm)	Vel (m/s)	Norm Vel (m/s)
Left Peroneal Motor - Lower (Ext Dig Brev)														
Ankle	NR		<6.6		>2.0				Fib head	Ankle		0.0		>41
Fib head	NR								Pop Fossa	Fib head		0.0		>41
Pop Fossa	NR													
Left Peroneal TA Motor - Lower (Tib Ant)														
B Fib Head		2.9	<4.2	5.3	>5.1	6.5	13.83	33.83	Poplit	B Fib Head	1.7	8.0	47	>41
Poplit		4.6	<6.8	4.7		5.7	11.88	29.15						
Left Tibial Motor - Lower (Abd Hall Brev)														
Ankle	NR		<6.1		>4.0				Knee	Ankle		0.0		>41
Knee	NR													

FIGURE 5: Upper and lower extremity motor nerve summary table

Reduced amplitude in motor nerves in the upper and lower extremities.

NR	F-Lat (ms)	Lat Norm (ms)	L-R F-Lat (ms)	L-R Lat Norm
Left Median (Mrkrs) (Abd Poll Brev)				
NR		<33		<2.2
Left Ulnar (Mrkrs) (Abd Dig Min)				
	30.83	<36		<2.5

FIGURE 6: F-wave studies

F-waves are absent. They are not recordable in the lower extremities and median nerve and are reduced in the ulnar nerve.

Discussion

The diagnosis of our case is challenging due to incomplete and overlapping manifestations of characteristic features of Miller-Fisher syndrome. Our patient did not present with ophthalmoplegia, and severe quadriplegia made it hard to examine or mask cerebellar dysfunction. Instead, the presentations of our patient resembled locked-in syndrome with preserved consciousness, intact eye range of motion, bulbar

weakness, and quadriplegia. However, his imaging studies did not show any structural lesions in the brain, brain stem, or cervical spine to explain the clinical features. Areflexia of the lower extremities led us to suspect a peripheral etiology, which is supported by his nerve conduction study. Alongside the positive anti-GQ1b antibody, the diagnosis of Miller-Fisher syndrome was made, and plasma exchange started. The patient responded well to the treatment, and his muscle strength improved significantly in both limbs and the face.

Bulbar symptoms are not part of the triad of typical MFS but may be more common than we thought and are easily overlooked. In a case series report, seven out of 15 patients had bulbar palsy [5]. A wide range of clinical manifestations other than typical Miller-Fisher syndrome have been reported in patients with positive anti-GQ1b antibodies, including Bickerstaff brainstem encephalitis, Guillain-Barré syndrome, pharynx-neck-brachial muscle weakness, and acute ophthalmoparesis without ataxia [2]. A positive anti-GQ1b antibody can be identified in 86.5% of patients with MFS, 74% of patients with BBE, and 73% of patients with GBS with ophthalmoplegia, based on a previous report [6]. The case we presented here is quite unusual, with profound bulbar and limb weakness without ophthalmoplegia. Similar clinical presentations and nerve conduction studies can be seen in acute motor sensory axonal neuropathy (AMSAN), another variant of GBS. Positive antiganglioside antibodies can also be seen in AMSAN, but mostly anti-GM1b and anti-GD1a IgG, as well as anti-GM1 IgG. So far, no case report of AMSAN has presented with a positive anti-GQ1b antibody. Thus, our case supported more of the concept that the diagnosis of those overlap syndromes may be better based on antibodies rather than clinical manifestations.

Patients with anti-GQ1b antibody syndrome may have a preceding infection, most commonly upper respiratory infection and acute gastroenteritis [7]. The neurological symptoms that occurred after an *Escherichia coli* infection, in our case, are uncommon. We only found one previous case report in the literature review with a similar *E. coli* infection [8]. Like most MFS patients, our patient responded well to treatment with a good recovery. The diagnosis of MFS or related disorders such as BBE can be challenging and still controversial due to the myriad of atypical and overlapping forms; thus, the term “anti-GQ1b antibody syndrome” has been introduced [2] to gain a better understanding of the etiological relationship among those patients. With the addition of our case report, it helps further expand the clinical spectrum of anti-GQ1b antibody syndrome.

## Conclusions

Diagnosis of MFS and associated disorders can be challenging due to multiple clinical variants of anti-GQ1b antibody syndrome. A positive serum antibody titer can aid in the diagnosis. Early recognition is important due to favorable responses to treatment.

## Additional Information

### Disclosures

**Human subjects:** Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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